

Clinical features in mild type and severe type of COVID-19 patients

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Abstract

Background: Coronavirus Disease 2019 (COVID-19) outbreak in Wuhan and spread to the world quickly. We aim to describe the clinical features and compare them between mild type and severe type of COVID-19 patients.

Methods: Laboratory confirmed COVID-19 patients were included in this study. Patients' demographic data and clinical features were recorded and compared between mild type and severe type.

Results: Fifteen patients were confirmed COVID-19 and enrolled in this study. Six patients were of mild type, while 9 patients were of severe type. Statistical differences were found between mild type and severe type patients in retirement, epidemiological history, baseline blood level of lactate dehydrogenase and Oxygenation Index (All $p < 0.05$). All patients had ground-glass opacities without consolidation in initial chest computed tomography images, 2 (16.7%) patients had pulmonary nodules. There were no statistical differences between mild type and severe type patients in initial chest CT findings (All $p > 0.05$).

Conclusions: Differences can be found in baseline clinical features between mild type and severe type of COVID-19 patients to help health care providers making early judgement to the severity and proper treatment.

Trial registration: The study was registered in ClinicalTrials.gov, NCT04279782. Registered 20 February 2020 - Retrospectively registered, <https://clinicaltrials.gov/ct2/show/NCT04279782?term=NCT04279782&draw=2&rank=1>

Background

In December 2019, a series of pneumonia cases with unknown etiology were reported in Wuhan city, Hubei province, China ^[1]. Soon after that, World Health Organization (WHO) reported this situation ^[2, 3]. Gene sequencing analysis of the lower respiratory tract samples from the patients indicated a novel coronavirus ^[4]. The novel coronavirus was similar to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) ^[5] and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) ^[6]. It was officially named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 infection was called Coronavirus Disease 2019 (COVID-19) and spread to the world quickly. A total of global 4593 confirmed COVID-19 cases, of which 4537 were from China, had been reported by January 28, 2020 ^[7]. COVID-19 was declared as a global health emergency by WHO on January 30, 2020. The death rate was about 4.08% (3331 deaths out of 81740 cases) in People's Republic of China ^[8], 12.63% (17127 deaths out of 135586 cases) in Italy ^[9], and 2.69% (8910 deaths out of 330891 cases) in United States of America ^[10]. There have been 1279722 confirmed cases of COVID-19 in 211 countries, including 72616 (5.67%) deaths, reported to WHO on April 7, 2020 ^[11].

As death rate reached 5.67% globally, it is very important to make early diagnosis, early judgement to the severity and proper treatment to COVID-19 patients. An early prospective study analyzed clinical features of 41 confirmed COVID-19 patients in Wuhan and demonstrated that COVID-19 resulted in intensive care unit (ICU) admission (13 of 41 [32%] patients) and death (6 of 41 [15%] patients) ^[12]. Some symptoms, signs and laboratory tests were found to be predictors for ICU care patients. Otherwise, all 41 patients had abnormal findings on chest computed tomography (CT), with bilateral abnormal lung opacities. Chung et al ^[13] and Song et al ^[14] also demonstrated that ground-glass opacities (GGO) were found in initial chest CT images from most of the patients. As GGO are usually seen in other viral pneumonia and immune lung injury, it is difficult to distinguish COVID-19 from them in early stage. It is unknown whether the initial chest CT findings can make early judgement to the severity of COVID-19. According to COVID-19 guideline from People's Republic of China ^[15], patients can be divided into mild type and severe type (even critical type). Early judgement and proper treatment to these two types are urgent in clinical practice. More data from COVID-19 patients is needed as little is known about it.

In this study, we aim to describe epidemiological, clinical, laboratory, and radiological characteristics of COVID-19 patients. We also aim to compare the clinical features between mild type and severe type patients, helping health care providers to make early judgement to the severity and proper treatment. We hope our study findings will be supplementary data to COVID-19 and its clinical features ever known.

Methods

Patients

According to COVID-19 guideline ^[15], suspected COVID-19 patients were admitted to isolation unit, Department of Infectious Diseases of Third Affiliated Hospital of Sun Yat-sen University after procedures of consultation, discussion and decision from an expert team of three professors. Oropharyngeal swabs of the patients were obtained and sent to Center for Disease Control and Prevention (CDC) of Guangzhou city for detection the SARS-CoV-2 ribonucleic acid (RNA) after their admission immediately. Diagnosis of COVID-19 was confirmed if the detection result from CDC was positive. Laboratory confirmed COVID-19 patients were included in this prospective study registered in ClinicalTrials.gov (registration number NCT04279782, date February 20, 2020). This study was approved by the institutional review board (IRB) of Third Affiliated Hospital of Sun Yat-sen University (Ethics Committee reference number [2020]-02-019-01). All patients voluntarily signed an informed consent form approved by the IRB before participation.

Data Collection

Patients' demographic data and clinical data were recorded. Clinical data includes epidemiological history, past history, personal history, symptoms, signs, blood cells count, biochemical test results, and chest CT images.

Severe Type And Mild Type Definition

Severe type was defined as the patient met one of the following criteria ^[15]: respiratory rate ≥ 30 breaths per minute, pulse oxygen saturation (SpO_2) $\leq 93\%$ without oxygen support therapy, or Oxygenation Index (arterial partial pressure of oxygen to fraction of inspiration oxygen [$\text{PaO}_2/\text{FiO}_2$]) ≤ 300 mmHg.

Mild type was defined as the patient did not meet any of the criteria for severe type mentioned above.

Criteria For Discharge

Patients would be discharged if they met all of the following criteria ^[15]: normal body temperature maintaining for 3 days, obvious improvement of respiratory symptoms, absorption of inflammation in chest radiographic manifestation and two negative results of detecting SARS-CoV-2 RNA from respiratory samples with an interval of more than 24 hours.

Statistical Analysis

Continuous data were indicated with the mean \pm standard deviation (SD) while categorical data were reported with number and percentage (%). Student's independent t-test was used to compare the means between the two groups. If normality was not assumed, nonparametric test by using Mann-Whitney test would be used. Categorical results were compared by Chi-square test or Fisher's exact test (if expected value < 5 was found). The statistical significance level for all the tests was set at a P value < 0.05 . Statistical analyses were performed using IBM SPSS version 19 (SPSS Statistics V19, IBM Corporation, Somers, New York, USA).

Results

Baseline characteristics

A total of 106 suspected patients were admitted to isolation unit from January 22nd 2020 to April 6th 2020. Fifteen patients (9 males and 6 females) were confirmed COVID-19 and enrolled in this study. The average age of the 15 COVID-19 patients was 43.6 ± 13.4 years, and days from symptom onset to admission were 3.8 ± 2.3 . Fourteen (93.3%) patients had a fever. Other symptoms included fatigue, myalgia, cough, sputum production, sore throat, dry throat, chest tightness and diarrhea. Six patients were of mild type, while 9 patients were of severe type. No patients retired in mild type, while 5 (55.5%) patients retired in severe type ($p < 0.05$). Epidemiological history showed no patients were Hubei residents in mild type, while 6 (66.7%) patients were Hubei residents in severe type ($p < 0.05$). Respiratory rate was 18.0 ± 1.3 breaths per minute in mild type patients and 22.2 ± 5.8 breaths per minute in severe type patients ($p < 0.05$). No statistical differences were found between mild and severe type patients in age, sex, smoking history, days from onset to admission, fever, highest body temperature, fatigue, myalgia, cough, sputum

production, sore throat, dry throat, chest tightness, heart rate, systolic pressure, diastolic pressure or comorbidity. Baseline characteristics of COVID-19 patients were shown in Table 1.

Table 1
Baseline characteristics of COVID-19 patients

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Age, years	39.3 ± 7.7	46.4 ± 16.0	43.6 ± 13.4	0.555 ^a
≤ 60	6 (100%)	5 (55.6%)	11 (73.3%)	0.103 ^b
> 60	0 (0%)	4 (44.4%)	4 (26.7%)	
Sex				1.000
Male	4 (66.7%)	5 (55.6%)	9 (60%)	
Female	2 (33.3%)	4 (44.4%)	6 (40%)	
Occupation				0.044
Staff	6 (100%)	4 (44.4%)	10 (66.7%)	
Retirement	0 (0%)	5 (55.6%)	5 (33.3%)	
Smoking history	2 (33.3%)	2 (22.2%)	4 (26.7%)	1.000
Epidemiological history				0.036
Hubei resident	0 (0%)	6 (66.7%)	6 (40%)	
Travel to Hubei	2 (33.3%)	1 (11.1%)	3 (20%)	
Exposure to infected patient	4 (66.7%)	2 (22.2%)	6 (40%)	
Days from onset to admission	3.8 ± 2.4	3.8 ± 2.3	3.8 ± 2.3	0.947
Symptoms and signs				
Fever	5 (83.3%)	9 (100%)	14 (93.3%)	0.400
Highest body temperature, °C	37.88 ± 0.67	38.38 ± 0.53	38.18 ± 0.62	0.135 ^a
36.0-37.2	1 (16.7%)	0 (0%)	1 (6.7%)	0.534 ^b
37.3-38	2 (33.3%)	3 (33.3%)	5 (33.3%)	
38.1-39	3 (50%)	5 (55.6%)	8 (53.3%)	
> 39	0 (0%)	1 (11.1%)	1 (6.7%)	

^a: for continuous data

^b: for categorical data

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Fatigue or Myalgia	1 (16.7%)	5 (55.6%)	6 (40%)	0.287
Cough	3 (50%)	5 (55.6%)	8 (53.3%)	1.000
Sputum production	3 (50%)	1 (11.1%)	4 (26.7%)	0.235
Sore throat	1 (16.7%)	0 (0%)	1 (6.7%)	0.400
Dry throat	1 (16.7%)	3 (33.3%)	4 (26.7%)	0.604
Chest tightness	3 (50%)	1 (11.1%)	4 (26.7%)	0.235
Diarrhea	1 (16.7%)	1 (11.1%)	2 (13.3%)	1.000
Heart rate, beat per minute	90.7 ± 13.5	95.1 ± 10.3	93.3 ± 11.4	0.481 ^a
60 ~ 100	5 (83.3%)	5 (55.6%)	10 (66.7%)	0.580 ^b
> 100	1 (16.7%)	4 (44.4%)	5 (33.3%)	
Respiratory rate, breath per minute	18.0 ± 1.3	22.2 ± 5.8	20.5 ± 5.0	0.046 ^a
12 ~ 20	6 (100%)	6 (66.7%)	12 (80%)	0.229 ^b
> 20	0 (0%)	3 (33.3%)	3 (20%)	
Systolic pressure, mm Hg	141.0 ± 20.3	127.0 ± 17.2	132.6 ± 19.1	0.173 ^a
90 ~ 120	1 (16.7%)	4 (44.4%)	5 (33.3%)	0.435 ^b
121 ~ 140	2 (33.3%)	3 (33.3%)	5 (33.3%)	
> 140	3 (50%)	2 (22.2%)	5 (33.3%)	
Diastolic pressure, mm Hg	81.8 ± 9.5	80.6 ± 16.7	81.1 ± 13.8	0.868 ^a
60 ~ 80	4 (66.7%)	4 (44.4%)	8 (53.3%)	0.683 ^b
81 ~ 90	1 (16.7%)	3 (33.3%)	4 (26.7%)	
> 90	1 (16.7%)	2 (22.2%)	3 (20%)	
Comorbidity				
Hypertension	1 (16.7%)	3 (33.3%)	4 (26.7%)	0.604

^a: for continuous data

^b: for categorical data

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Chronic liver disease	1 (16.7%)	2 (22.2%)	3 (20%)	1.000
Hyperthyroidism	1 (16.7%)	0 (0%)	1 (6.7%)	0.400
Hyperlipidemia	0 (0%)	1 (11.1%)	1 (6.7%)	1.000
a: for continuous data				
b: for categorical data				

Baseline Laboratory Test Results

From the baseline laboratory test results, there were 6 (100%) patients with normal blood level of lactate dehydrogenase in mild type and 4 (44.4%) patients in severe type ($p < 0.05$). The Oxygenation Index was 511.2 ± 95.2 mm Hg in mild type patients and 358.5 ± 121.5 mm Hg in severe type patients ($p < 0.05$). No statistical differences were found between mild and severe type patients in normal blood cell count, or normal blood level of aspartate aminotransferase, alanine aminotransferase, albumin, total bilirubin, blood urea nitrogen, creatinine, creatine kinase, myoglobin, pro-brain natriuretic peptide, cardiac troponin I, prothrombin time, prothrombin time - international normalized ratio, procalcitonin, C-reactive protein, erythrocyte sedimentation rate, or PaO₂. Baseline laboratory results of COVID-19 patients were shown in Table 2.

Table 2
Baseline laboratory results of COVID-19 patients

	Mild type N = 6	Severe type N = 9	All N = 15	P value
White blood cell, × 10 ⁹ /L	5.36 ± 1.62	6.07 ± 1.67	5.79 ± 1.63	0.432
Lymphocyte, × 10 ⁹ /L	1.16 ± 0.36	1.68 ± 0.82	1.47 ± 0.71	0.173 ^a
≥ 1	4 (66.7%)	7 (77.8%)	11 (73.3%)	1.000 ^b
< 1	2 (33.3%)	2 (22.2%)	4 (26.7%)	
Red blood cell, × 10 ¹² /L	4.95 ± 0.72	4.62 ± 0.43	4.75 ± 0.56	0.283
Hemoglobin, g/L	141.8 ± 21.6	143.2 ± 10.7	142.7 ± 15.3	0.870
Platelet, × 10 ⁹ /L	217.3 ± 49.5	187.6 ± 56.4	199.5 ± 54.0	0.313
Aspartate aminotransferase, U/L				1.000
≤ULN*	5 (83.3%)	7 (77.8%)	12 (80%)	
>ULN	1 (16.7%)	2 (22.2%)	3 (20%)	
Alanine aminotransferase, U/L				1.000
≤ULN	4 (66.7%)	7 (77.8%)	11 (73.3%)	
>ULN	2 (33.3%)	2 (22.2%)	4 (26.7%)	
Albumin, g/L	48.7 ± 4.2	46.3 ± 5.5	47.3 ± 5.0	0.393
Total bilirubin, μmol/L				/
≤ULN	6 (100%)	9 (100%)	15 (100%)	
>ULN	0 (0%)	0 (0%)	0 (0%)	
Blood urea nitrogen, mmol/L				1.000
≤ULN	6 (100%)	8 (88.9%)	14 (93.3%)	

^a: for continuous data

^b: for categorical data

*: ULN, upper limit of normal

	Mild type N = 6	Severe type N = 9	All N = 15	P value
>ULN	0 (0%)	1 (11.1%)	1 (6.7%)	
Creatinine, $\mu\text{mol/L}$				1.000
$\leq\text{ULN}$	6 (100%)	8 (88.9%)	14 (93.3%)	
>ULN	0 (0%)	1 (11.1%)	1 (6.7%)	
Creatine kinase, U/L				0.604
$\leq\text{ULN}$	5 (83.3%)	6 (66.7%)	11 (73.3%)	
>ULN	1 (16.7%)	3 (33.3%)	4 (26.7%)	
Lactate dehydrogenase, U/L				0.044
$\leq\text{ULN}$	6 (100%)	4 (44.4%)	10 (66.7%)	
>ULN	0 (0%)	5 (55.6%)	5 (33.3%)	
Myoglobin, $\mu\text{g/L}$				/
$\leq\text{ULN}$	6 (100%)	9 (100%)	15 (100%)	
>ULN	0 (0%)	0 (0%)	0 (0%)	
Pro-brain natriuretic peptide, pg/mL				1.000
$\leq\text{ULN}$	6 (100%)	8 (88.9%)	14 (93.3%)	
>ULN	0 (0%)	1 (11.1%)	1 (6.7%)	
Cardiac troponin I, ng/mL				0.400
$\leq\text{ULN}$	5 (83.3%)	9 (100%)	14 (93.3%)	
>ULN	1 (16.7%)	0 (0%)	1 (6.7%)	
arterial partial pressure of oxygen, mm Hg	116.1 \pm 37.8	87.4 \pm 17.6	98.9 \pm 30.0	0.067
Oxygenation Index, mm Hg	511.2 \pm 95.2	358.8 \pm 121.5	419.7 \pm 132.8	0.023
Prothrombin time, second	12.70 \pm 0.28	12.91 \pm 0.36	12.83 \pm 0.33	0.242

^a: for continuous data

^b: for categorical data

*: ULN, upper limit of normal

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Prothrombin time - international normalized ratio	0.95 ± 0.02	0.97 ± 0.03	0.96 ± 0.03	0.139
Procalcitonin, ng/mL				/
≤ 0.5	6 (100%)	9 (100%)	15 (100%)	
> 0.5	0 (0%)	0 (0%)	0 (0%)	
C-reactive protein, mg/L				0.329
≤ULN	3 (50%)	2 (22.2%)	5 (33.3%)	
>ULN	3 (50%)	7 (77.8%)	10 (66.7%)	
Erythrocyte sedimentation rate, mm/H				1.000
≤ULN	3 (50%)	5 (55.6%)	8 (53.3%)	
>ULN	3 (50%)	4 (44.4%)	7 (46.7%)	
^a : for continuous data				
^b : for categorical data				
*: ULN, upper limit of normal				

Initial Chest CT Image Findings

In initial chest CT images, unilateral involvement was found in 3 (20%) patients, bilateral involvement was found in the rest 12 (80%) patients. Only one lobe was involved in 2 (13.3%) patients, multi-lobes were involved in the rest 13 (86.7%) patients. The right upper lobe and right middle lobe were involved in 8 (53.3%) patients, the right lower lobe and left upper lobe were involved in 10 (66.7%) patients, the left lower lobe was involved in 11 (73.3%) patients. All patients had GGO without consolidation, 2 (13.3%) patients had pulmonary nodules. Pulmonary Fibrosis, pulmonary emphysema, cavitation, pleural effusion and lymphadenopathy were absent. Initial chest CT findings of COVID-19 patients were shown in Table 3. No statistical differences were found between mild and severe type patients in initial chest CT findings. Initial chest CT images of the 9 severe type patients were shown in Fig. 1.

Table 3
Initial chest CT findings of COVID-19 patients

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Lateral				0.525
Unilateral	2 (33.3%)	1 (11.1%)	3 (20%)	
Bilateral	4 (66.7%)	8 (88.9%)	12 (80%)	
Number of lobes affected				0.155
1 lobe affected	2 (33.3%)	0 (0%)	2 (13.3%)	
2 lobes affected	1 (16.7%)	2 (22.2%)	3 (20%)	
3 lobes affected	0 (0%)	4 (44.4%)	4 (26.7%)	
4 lobes affected	1 (16.7%)	2 (22.2%)	3 (20%)	
5 lobes affected	2 (33.3%)	1 (11.1%)	3 (20%)	
Lobe affected				
Left upper lobe	3 (50%)	7 (77.8%)	10 (66.7%)	0.329
Left lower lobe	5 (83.3%)	6 (66.7%)	11 (73.3%)	0.604
Right upper lobe	3 (50%)	5 (55.6%)	8 (53.3%)	1.000
Right middle lobe	3 (50%)	5 (55.6%)	8 (53.3%)	1.000
Right lower lobe	4 (66.7%)	6 (66.7%)	10 (66.7%)	1.000
Lesion manifestation				
Ground-glass opacities without consolidation	6 (100%)	9 (100%)	15 (100%)	/
Consolidation without ground-glass opacities	0 (0%)	0 (0%)	0 (0%)	/
Ground-glass opacities with consolidation	0 (0%)	0 (0%)	0 (0%)	/
Pulmonary fibrosis	0 (0%)	0 (0%)	0 (0%)	/
Pulmonary emphysema	0 (0%)	0 (0%)	0 (0%)	/

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Pulmonary nodules	0 (0%)	2 (22.2%)	2 (13.3%)	0.486
Cavitation	0 (0%)	0 (0%)	0 (0%)	/
Pleural effusion	0 (0%)	0 (0%)	0 (0%)	/
Lymphadenopathy	0 (0%)	0 (0%)	0 (0%)	/

Treatment And Current Clinical Outcome

All COVID-19 patients received antiviral therapy. Twelve (80%) patients received oral arbidol. Fifteen (100%) patients received oral lopinavir and ritonavir. Four (26.7%) patients received interferon alfa-2b inhalation. Thirteen (86.7%) patients received antibiotics therapy. Four (26.7%) patients received corticosteroid and human immunoglobulin intravenous injection. Two (13.3%) patients received thymosin α 1 subcutaneous injection. Twelve (80%) patients received oxygen support therapy. One (6.7%) patient needed care in ICU. Days from symptom onset to undetectable SARS-CoV-2 RNA were 20.5 ± 12.1 . Days from admission to undetectable SARS-CoV-2 RNA were 16.7 ± 11.6 . No statistical differences were found between mild and severe type patients in days from symptom onset to undetectable SARS-CoV-2 RNA or days from admission to undetectable SARS-CoV-2 RNA. Fourteen (93.3%) patients recovered and discharged. One (6.7%) patient was receiving treatment in hospital currently. Treatment and current clinical outcome of COVID-19 patients were shown in Table 4.

Table 4
Treatment and current clinical outcome of COVID-19 patients

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Drugs				
Antiviral therapy	6 (100%)	9 (100%)	15 (100%)	/
Arbidol	3 (50%)	9 (100%)	12 (80%)	0.044
Lopinavir and Ritonavir	6 (100%)	9 (100%)	15 (100%)	/
Interferon alfa-2b inhalation	0 (0%)	4 (44.4%)	4 (26.7%)	0.103
Antibiotics therapy	4 (66.7%)	9 (100%)	13 (86.7%)	0.143
Levofloxacin	3 (50%)	1 (11.1%)	4 (26.7%)	0.235
Moxifloxacin	1 (16.7%)	8 (88.9%)	9 (60%)	0.011
Cefoperazone	0 (0%)	2 (22.2%)	2 (13.3%)	0.486
Meropenem	0 (0%)	1 (11.1%)	1 (6.7%)	1.000
Teicoplanin	0 (0%)	3 (33.3%)	3 (20%)	0.229
Linezolid	0 (0%)	1 (11.1%)	1 (6.7%)	1.000
Use of corticosteroid	0 (0%)	4 (44.4%)	4 (26.7%)	0.103
Use of human immunoglobulin	0 (0%)	4 (44.4%)	4 (26.7%)	0.103
Use of thymosin α1	1 (16.7%)	1 (11.1%)	2 (13.3%)	1.000
Ambroxol	1 (16.7%)	5 (55.6%)	6 (40%)	0.287
Oxygen support				0.049
None	3 (50%)	0 (0%)	3 (20%)	
Nasal cannula	3 (50%)	4 (44.4%)	7 (46.7%)	

#: RNA, ribonucleic acid

*: only 8 patients of severe type were calculated, as the rest one was still hospitalizing in ICU from January 22nd, 2020.

	Mild type N = 6	Severe type N = 9	All N = 15	P value
Non-invasive ventilation	0 (0%)	4 (44.4%)	4 (26.7%)	
Invasive ventilation	0 (0%)	1 (11.1%)	1 (6.7%)	
Transfer to intensive care unit	0 (0%)	1 (11.1%)	1 (6.7%)	1.000
Days from onset to undetectable SARS-CoV-2 RNA [#]	15.7 ± 7.0	23.7 ± 14.1	20.5 ± 12.1	0.223
Days from admission to undetectable SARS-CoV-2 RNA	12.0 ± 5.5	19.8 ± 13.8	16.7 ± 11.6	0.216
Days from admission to discharge	19.2 ± 6.7	26.4 ± 8.6 [*]	23.3 ± 8.4 [*]	0.116
Current clinical outcome				1.000
Recovered and discharged	6 (100%)	8 (88.9%)	14 (93.3%)	
Stabilized and hospitalized	0 (0%)	1 (11.1%)	1 (6.7%)	
Death	0 (0%)	0 (0%)	0 (0%)	
[#] : RNA, ribonucleic acid				
[*] : only 8 patients of severe type were calculated, as the rest one was still hospitalizing in ICU from January 22nd, 2020.				

Discussion

This is a descriptive study on the clinical features of COVID-19 patients in Third Affiliated Hospital of Sun Yat-sen University located in Guangzhou city. Nine (60%) patients were of severe type, and one of them needed treatment in ICU and still hospitalized in ICU for more than 70 days (from January 22nd, 2020). This reminds us not to underestimate the severity of COVID-19. Early recognition and judgement to severe type of COVID-19 patients are urgent and important in clinical practice, in order to make proper treatment and reduce death rate.

Our study showed retirement, Hubei residents and faster respiratory rate were more frequent in severe type patients. It is consistent with the results from Huang's study^[12], which compared COVID-19 patients with ICU care and no ICU care. Other data, including age, sex, smoking history, comorbidity, symptoms and signs, were similar. Although age was of no statistical differences between the two types, the elderly was thought to be related to retirement, comorbidity and progression to severe type in clinical practice. Hubei residents seemed to be "first generation"^[16] or the next generation, infected with SARS-CoV-2 of

relative strong virulence, making infection much more severe than patients from other cities. The common symptoms in COVID-19 patients includes fever, fatigue, myalgia, sore throat, cough, sputum production, dyspnea. These symptoms were also reported by other studies [12, 17]. Close attention should be paid to symptom diarrhea, which may be evidence for digestive system impairment. SARS-CoV-2 RNA could be detected in blood and anal swab specimens [18], that the virus invades circulatory and digestive systems. ACE2 was reported as a receptor for coronavirus replication [19], as it was highly expressed in lung and intestine tissues. Whether SARS-CoV-2 could invade urinary system is still unknown, as urinary irritation symptoms and signs were absent in our study. More studies are needed.

In terms of baseline laboratory tests, higher blood level of lactate dehydrogenase and lower Oxygenation Index were demonstrated in severe type patients. Lactate dehydrogenase is one of the important enzymes for anaerobic glycolysis and gluconeogenesis. Its elevation prompts liver, lung, heart and kidney diseases. Oxygenation Index, an item of blood gas analysis, reflects oxygenation capability of tissue and organ. Respiratory dysfunction is indicated if the Oxygenation Index is less than 300 mm Hg. Other biochemical parameters for inflammation, liver function, coagulation function, cardiac function, renal function and pulmonary function were similar in two groups. Interestingly, lymphopenia is seen in both groups without statistical difference, as it could be used as a reference index in the diagnosis of COVID-19. Dynamic observation of lymphocyte count may be used as a reference index in degree of severity.

Initial chest CT images in our study demonstrated that ground-glass opacities without consolidation were found in all patients without specificity. Bilateral involvement was found in 12 (80%) patients and multi-lobes involvement was found in 13 (86.7%) patients. Similar findings were reported [13, 14]. It was difficult to distinguish COVID-19 from other pneumonia in early stage by initial chest CT images. As there were no statistical differences between mild and severe type patients in initial chest CT findings in our study, it also seemed to be difficult to distinguish the two types from each other by initial chest CT images. However, subsequent consecutive chest CT examinations are necessary to assure the change of pneumonia and make proper treatment.

COVID-19 lacks of confirmed effective antiviral treatment. All the experience is from treatment for SARS-CoV and MERS-CoV infection. Combination of lopinavir and ritonavir was clinical beneficial among SARS-CoV patients [20]. A placebo-controlled trial of interferon beta-1b, lopinavir and ritonavir among patients with MERS infection was initiated in Saudi Arabia [21]. As Remdesivir may have potent efficacy to treat MERS-CoV and SARS-CoV infections [22, 23], clinical trials of Remdesivir in COVID-19 were initiated in China. It is recommended to use intravenous immunoglobulin to enhance the ability of anti-infection for severe patients. Corticosteroids (methylprednisolone 1–2 mg/kg per day) are recommended to control inflammatory-induced lung injury for patients with acute respiratory deficiency syndrome for a short duration. Corticosteroids may be a double-edged sword as it did not have an effect on mortality, but rather delayed viral clearance [24–26]. Otherwise, antibiotics therapy, oxygen support therapy and symptomatic therapy are all needed in management of COVID-19. ICU care and vital support are urgent if vital signs are unstable. In our study, days from symptom onset to undetectable SARS-CoV-2 RNA were

20.5 ± 12.1, days from admission to undetectable SARS-CoV-2 RNA were 16.7 ± 11.6. A retrospective cohort study shown median duration of viral shedding was 20.0 days in survivors [27]. It indicated that SARS-CoV-2 invaded into human body and sustained for a long time, although antiviral therapy what we thought to be effective for SARS-CoV-2 was given to the patients. No statistical differences were found between mild and severe type patients in days from symptom onset to undetectable SARS-CoV-2 RNA or days from admission to undetectable SARS-CoV-2 RNA. The duration for positive SARS-CoV-2 RNA in the two types of patients was similar.

This study has several limitations. First, only fifteen COVID-19 patients were included without pediatrics or adolescent patients; suspected but exclusive diagnosed cases were ruled out in the analyses. Second, final clinical outcome of all patients was unavailable at the time of analysis. Third, changes of viral load and antibody titers were not available since the patients were confirmed diagnosed.

However, the patients enrolled in this study are treated in Guangzhou, giving new perspectives out of the origin city Wuhan in China. The data in this study permit an early assessment of clinical features of mild type and severe type patients with COVID-19.

Conclusions

Differences can be found in baseline clinical features in mild type and severe type patients with COVID-19. This helps health care providers to make early judgement to severe type patients and give proper treatment for them.

Abbreviations

WHO

World Health Organization

SARS-CoV

Severe Acute Respiratory Syndrome Coronavirus

MERS-CoV

Middle East Respiratory Syndrome Coronavirus

SARS-CoV-2

Severe Acute Respiratory Syndrome Coronavirus 2

COVID-19

Coronavirus Disease 2019

ICU

intensive care unit

CT

computed tomography

GGO

ground-glass opacities

CDC
Center for Disease Control and Prevention
RNA
ribonucleic acid
IRB
institutional review board
SpO₂
pulse oxygen saturation
PaO₂
arterial partial pressure of oxygen
FiO₂
fraction of inspiration oxygen
SD
standard deviation

Declarations

Ethic approval and consent to participate

This study was approved by the institutional review board (IRB) of Third Affiliated Hospital of Sun Yat-sen University (Ethics Committee reference number [2020]-02-019-01). The patient voluntarily signed an informed consent form approved by the IRB before participation.

Consent for publication

The patients voluntarily signed an informed consent form regarding publishing their data without their names and identification card numbers.

Availability of data and material

The data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests

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management, analysis, and interpretation of the data; preparation, writing, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author Contributions

All authors contributed to the concept and design. L P, J L and W X had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. W X, Q L, D C and Z L contributed to acquisition, analysis and interpretation of data. W X contributed to statistical analysis. W X and L P drafted the manuscript. L P and Z G obtained funding and took responsibility for the supervision. All authors read and approved the final manuscript.

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Figures

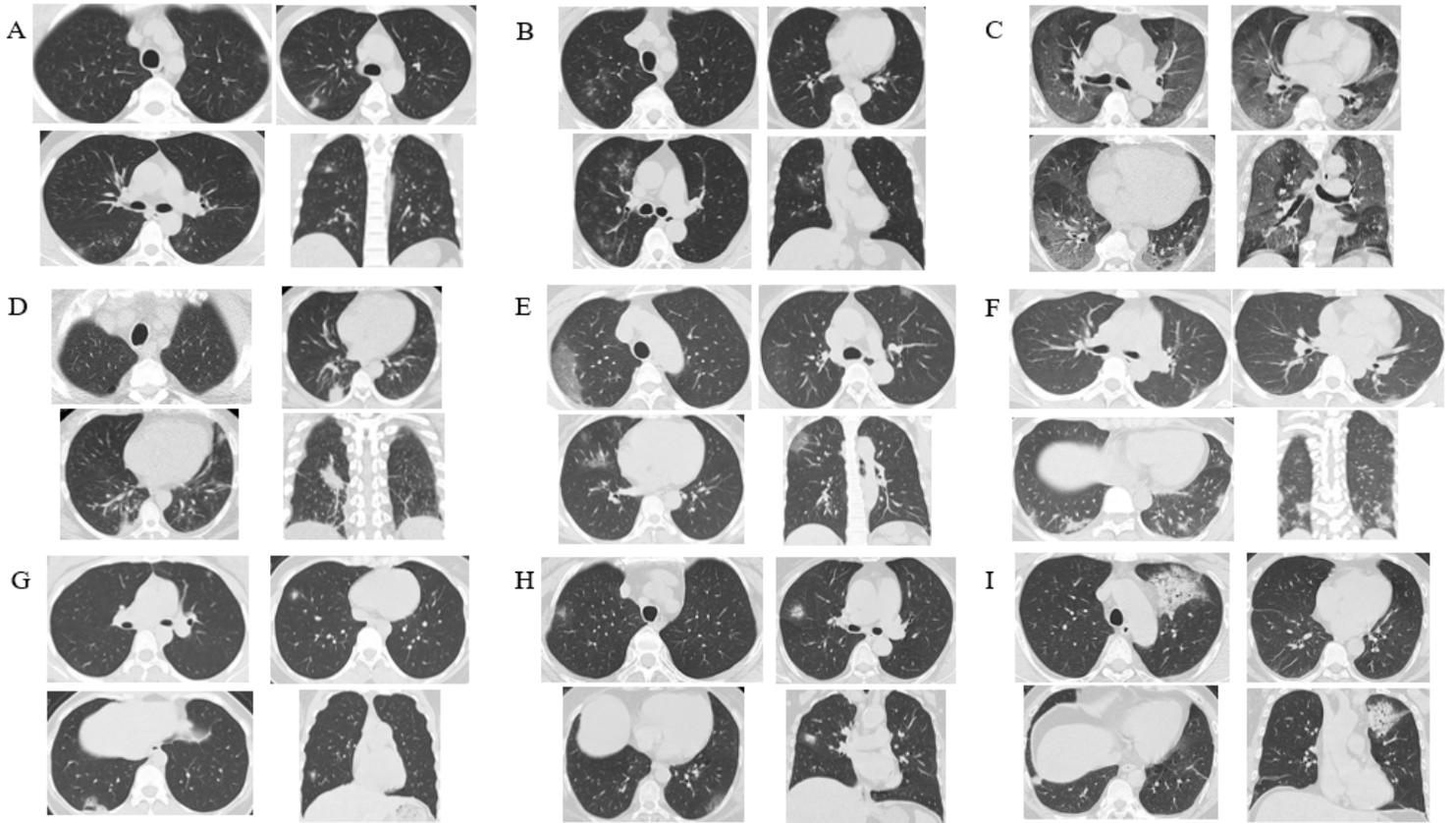


Figure 1

Initial chest CT images of the 9 severe type COVID-19 patients (A) 37-year-old male with exposure history to suspected patient, presenting with fever, cough and myalgia. Chest CT images show bilateral multiple lobular GGO on day 4 after symptom onset. (B) 64-year-old male who is a Wuhan resident, presenting with fever and myalgia. Chest CT images show unilateral multiple lobular GGO and pulmonary nodules on day 1 after symptom onset. (C) 61-year old male who is a Wuhan resident, presenting with fever, fatigue myalgia and cough, ultimately requiring intensive care unit admission. Chest CT images show diffuse bilateral multiple lobular GGO on day 6 after symptom onset. (D) 34-year-old male with travel history to Wuhan, presenting with fever, dry throat, myalgia and chest tightness. Chest CT images show bilateral multiple lobular GGO on day 2 after symptom onset. (E) 62-year-old female who is a Wuhan resident, presenting with fever, cough and dry throat. Chest CT images show bilateral multiple lobular GGO and pulmonary nodules on day 6 after symptom onset. (F) 27-year old female who is a Hubei resident, presenting with fever and fatigue. Chest CT images show bilateral multiple lobular GGO on day 4 after symptom onset. (G) 27-year-old female with exposure history to suspected patient, presenting with fever and dry throat. Chest CT images show bilateral multiple lobular GGO on day 1 after symptom onset. (H) 63-year-old female who is a Wuhan resident, presenting with fever and cough. Chest CT images show bilateral multiple lobular GGO on day 4 after symptom onset. (I) 43-year-old male who is a Hubei resident, presenting with fever, cough and sputum production. Chest CT images show bilateral multiple lobular GGO on day 7 after symptom onset.